ETHICAL DECISION MAKING IN COMMITTEE. THE ROLE OF REVIEW BOARDS AND ETHICS COMMITTEES IN HEALTH CARE, HEALTH POLICY AND MEDICAL RESEARCH

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Committees and responsabilities

From the crib to the grave: committees, committees, committees. Committees have become a part of our life; some of us are members of committees; all of us depend on decisions made or recommended by committees, we don't know and by members we don't know, - anonymous bodies, making decisions for others by majority vote. Our generation has seen the mushrooming of committees all over the world and for all possible issues, including committees for patient care in the hospital, for setting health care policy on the local, provincial or national level, for supervising the ethical practice of research on humans, for health education, and committees within professional groups and organizations in the nursing, medical, and researching professions.

What is the morale or the reason behind the culture of decision making by committee? Is there a higher authority of moral judgment if made by a group of people rather than by one individual? And, if committees make moral judgments and ethical decisions, will these committees also be morally or legally liable for decisions the same way a competent individual has to be hold liable morally and legally for her or his actions? And what is the personal moral or legal liability of individual members of committees; to whom to they owe responsibility: to nobody except to their individual conscience, or to those who elected them to be a member of that committee, or to the constituency they are expected to represent whether elected by that group or not? Personal experiences and empirical research suggest that the answer to these questions might rather be NO than YES. Each of these questions is full of philosophical, cultural and political complexities which we

cannot address in detail today; but it is important to keep these questions in mind in order to be aware that decision by committee is only one of many other model of deciding, accepting responsibility, setting rules, policy or strategy, drafting regulations or recommendations, distributing public or private funds, or making recommendations for policy options to other bodies.

Two arguments have been voiced to support the mushrooming of commissions and committees: (a) the need for *expert advice* in complex political, social, and interdisciplinary issues, and (b) the need for *participatory representation* of the stakeholders involved. Keeping the fragile nature of decision making and recommendation making in committee in mind, I will discuss three different types of committees in the area of health care: (a) commissions on the state or national or transnational level, (b) research review boards, required for human experimentation and innovative therapy, and (c) hospital ethics committees setting rules for hospitals or wards and focussing on individual patient's care.

Policy stting Committes on the provincial or state level

For commissions on the state level it is very important, that they focus (a) on identifying different views of the world and (b) on options for *societal consent* or on means to live with dissent, if consent cannot be achieved. Sometimes a commission has to deal with issues such as abortion for which the arguments pro and contra have been voiced for centuries, sometimes the analytical framework has not been constructed such as in the case of genetic screening or xenotransplantation. In both cases the commission has to provide analytical justification from first principles either for *consensus formation or for policy options* on how to live with dissent. The US National Commission's Belmont Report, for example, broke new intellectual grounds by identifying for a postmodern, pluralistic society the principles of autonomy, nonmaleficence, beneficence and justice as the leading first principles for establishing either consensus or reasoning in favor of acceptance of individually different positions in the respect of the dignity of the individual religious or moral conscience. More fundamental, philosophical bioethical analysis - such as writing books on general theories of justice - is best done by those whose job is to think and write, not a group of commissioners selected because of their national prominence, professional background, political connections, and ideological affiliations.

An international, national or state committee can articulate others' positions, filter information, and facilitate communication among policy makers. Legally nonbinding *declarations* of high moral binding such as UNESCO's

declaration for the protection of the human genome are easier to be achieved and to become valid than *regulations* or *international conventions* such as the EU Bioethics Convention which still needs to jump the parliamentary hurdles of some countries and need transformation into national law. Given the fact that declarations and regulations in bioethics all are targeted at protecting the individual fellow human as a person and as persons happen to and have every right to disagree, there are certain limits as to what can be declared and regulated. Among the number of goals and means of policy oriented ethics committees, let us briefly discuss the following nine [see also R Cook-Deegan, in: Sass 1988]:

(1) Searching for a compromise: Some public issues arise so quickly that controversy surfaces as a symptom of incomplete analysis by different factions. In such cases, there is an opportunity to articulate a position that could be widely accepted. In political terms, this is extremely useful because democratic government is erected on consensus, although constrained by unalienable individual rights, as the philosophers of the Age of Reason have stressed. Human gene therapy is an example: consensus that somatic cell gene therapy is little different form other medical technologies was voiced first by the US President's Commission and then by the US Congress Office of Technology. This was sufficient to prevent legislation to prohibit or limit it. The US President's Commission report on defining death, and many of the US National Commission's reports on human research subjects also exemplify this function of forming the point of condensation for consensus. Consensus formation is ideally suited to national commissions or ad hoc commissions. The fundamentals of religions and worldviews might be quite different and exclusive to each other, but as Jesus has demonstrated in the parable of the Good Samaritan, there are certain mid-level ethical principles, such as solidarity, reciprocity, 'neighbor's love', that can be shared by many different ideational commitments.

(2) Clarification of values and understanding of disagreements: Consensus does not always form around issues, even when a technology is the main new feature. Nuclear power and arms control have not been notable for their rational public discourse or clean and highly analytical policy process. In bioethics commissions, the objective may be consensus but the result may be incompatible views, as we have seen in the debates on abortion and most recently on stem-cell research. The process of articulating dissent is nonetheless valuable. Seeking consensus may also contribute to public debate with no expectation that concrete recommendations are possible. Thus consensus-seeking need not be considered a failure if it yields progress but no end. There is ample value in ventilating disparate moral positions publicly. An illusory or

forced consensus can result in policy change only to breed later backlash as the policy encounters resistance. The classical ethical principle to govern a procedural proposal rather than a content solution is the principle of *subsidiarity*, the rule, that at the lowest possible societal level and by those most directly involved decision should be made, and that larger societal or political bodies should only take action when individuals and groups most directly involved demonstrate that they are unable to solve conflicts or provide help and support to those in need. In socialethics, this principle has proven to be of great value; elsewhere I have recommended that its use should be tested in bioethics also.

(3) Identifying emerging issues: National commissions can identify future issues. This can be quite helpful to policy makers even if no conclusions are reached about options for dealing with the issues. "Early warning" functions constitute specific, narrow, example of consensus formation. The focus is on identifying issues likely to matter in the future rather than on solutions to current policy concerns. If a set of issues is agreed to be important in the future, then a politician can begin to formulate his or her positions on those issues, and to commit resources to finding out about them. In Germany, we basically had not much public debate or a national ethics committee studying the impact of nuclear energy on attitudes and individual and group risk assessment; unfortunately only later we had those debates, when billions of Deutsche Mark had already been employed and when nuclear energy facilities were already in use.

(4) Mitigating a societal debate and probable consensus: If an issue very new to the public and to experts and politicians, public policy as well as public discourse may very well benefit from a debate that pits the best minds of various camps against one another in a mutually respecting forum. More often, however, little value will be added by the commission's deliberations. Fetal research is an example of an issue that has been addressed by the US National Commission, then an Ethics Advisory Board, and was to be addressed by BEAC (US Bioethics Advisory Council). No action to break up the ideological logjam has been effective.

Even if consensus is not possible, a softening of positions at the extreme edges may be. If this occurs, the environment for making tough policy choices may be less threatening, and incremental policy adjustments may become possible. Some issues bound to elude consensus are relatively easy to identify. They usually have been hotly debated for years (e.g., human rights, fetal research, abortion, access to health care, surrogate motherhood, homosexuality, cloning, organs for sale). Changes on such issues require either extended careful thought, followed by changes in public attitudes, or classical political maneuvering to which ethical analysis contributes little. If continuing a controversial debate is the objective, there is generally little to be gained by having a national commission.

Successful as a means and as a moderator for public discourse were two national commissions in Denmark, one addressing the issue of brain-death, the other acceptance and validation of Advance Medical Directives. Both initiatives went over a few years and funds were disbursed for supporting a debate in the academia, in neighborhoods, in churches and organizations; only after such an extended debate initiated, but not moderated or controlled by the commission, the Danish parliament was ready to pass legislation on both issues.

(5) Camouflaging governmental desinterest or inaction resulting in postponement of issues: It is quite common for politicians to be evasive or cowardice in regard to making hard choices in the public's best interest, such as in health care finance reform or in social security and old-age pension issues. The choices to be made are mostly unpopular and to not win immediate support; but immediate support and success is important for politicians depending on the electorate's vote. To install a blue-ribbon committee or an expert group for further studies is a widely used tool to postpone or to neglect decisions. Members of those committees are in quite difficult professional and ethical position: on one side they are allowed and asked to contribute their visions, ideas and expertise, and on the other side they very clearly recognize that most likely nothing will come out of their work, that they are actually contributing to increasing problems by putting them on the back-burner.

Politicians often hope that controversies will go away. They may seek to use a 'study' or a 'committee' as a delaying tactic, judging that the intensity of conflict will dissipate over the course of a mandated study. A closely related tactic is for politicians to call for a study, while politically maneuvering to distance themselves from its results. When the results are produced, they can accept the results they agree with, and blame the commission for those they reject.

(6) Proposing Regulations or Drafting Legislation: A committee can, having identified an existing consensus, devise a way to incorporate it into practice. In the US, the President's Commission served this role in a multitude of issues. Its report on 'Defining Death' served this function, as the template for statutes passed in the States. The US National Commission reports on children, prisoners, and other vulnerable populations were readily translated into federal regulations governing research. In Congress, this function is usually performed by committees, which have access to outside expertise and focus it on legislation. Executive agencies also have policy-making groups that perform analogous functions. From time to time, however, policy makers may wish to attend explicitly to the ethical dimensions of a policy choice. In such cases, a national committee or ad hoc panel is the logical choice. In Germany, we have so-called Enquete-Commissions for genetic technologies, instituted by and reporting to the national parliament.

(7) Creating and Providing a Critical Mass of Ethical Experts: Ethics Committees serve as educational means in interdisciplinary, academia-public, and theory-practice interaction and experience of members of different professional and social background. It is not easy to find philosophers who despite their expertise in one or the other field of philosophy are capable of finding the common language and method of working in a team of physicians, regulators, lawyers and scientists. The same is true of the other professions. Interdisciplinary committees are the best breeding ground for crossdisciplinary understanding and evaluating.

A societal effort to incorporate ethical analysis into public policy rests on an academic reservoir of technical experts, legal scholars, and humanists. If no critical mass of people in these fields exists, then the first step in any program must be to develop one. Grants and training programs are the direct means to this end. If there is sufficient expertise in the various fields, then ad hoc committees, state committees, or permanent review boards are all possibilities. Choosing among these options will depend on the number of issues at hand, the resources available, and the objectives of seeking advice.

If consensus is a likely outcome, and publicity is desirable, then an independent blue ribbon committee is the logical choice. Care must be taken, however, to provide sufficient budget and time. Funds and schedules must, in particular, allow for the extensive network formation necessary for a proper job. If there are many issues and the decision making apparatus is complex, then a permanent analytical agency is the option of choice. In this case, the extra investment in a management structure is necessary in addition to the report-writing team or teams.

(8) Debating and Confronting Special Interest Group Lobbying: The modern world of public policy and public discourse is not only influenced by committees of various kind, even more so by lobby groups and special interest groups, actually dominating those issues of their specific interest. Interest groups have become much more sophisticated in their use of national direct mail fund-raising, organization of national letter-writing campaigns, boycotts, and other tactics. They have introduced a new dynamic into the political process. They are organized around specific issues, and establish a staff, newsletters, policy analysis mechanisms, and capacities for political strategy that once formed can be applied to new issues as they arise. The great strength of interest groups is their narrow focus, which permits them to concentrate on a specific agenda. But this can also be a weakness, as it tends to result in fixed policy positions that once taken are extremely difficult to modify. A narrow focus can lead to parochial policy formulations; consequences of policy recommendations may not take account of their broader impact outside the sphere of interest and thus are not in the interest of the public and most likely will not last.

The abortion debate definitely is overdominated by special interest groups in all countries in Europe and the Americas; new areas for special interest groups are environment, genetic modification of cultured animals and plants, animal research, euthanasia, in vitro fertilization, cloning, and fetal and stem cell research.

(9) Special Roles for Provincial or other Ethics Committees on the Grass-root Level: As far as I see, not enough consideration has been given to the role of ethics committees initiating public moral discourse and debate and developing public policy options on the provincial level. In a politically coordinated Europe, the role of nation states will diminish, and so will the role and authority of national ethics committees. The role of European harmonization will be increased and as a counterpart to this, new roles and responsibilities should be developed for the provincial level. In Germany, we have quite a difference of priorities in public culture and moral concern in more religiously oriented states such as Bavaria and more secular cultures such as in the northern part of Germany. Other nation states have similar differences based on tradition and attitude in different provinces and areas of the country. As we have seen, e.g. the availability of organ-sharing has increased, since information, education and promotion of organ donation has been concentrated on the provincial level.

This is a list of issues, where societal ethics committees on a provincial level close to the individuals and institutions they serve can have an impact on consensus formation and the improvement of ethical quality in political, professional and institutional decision making: (1) access to long-term care; (b) financing health care; (3) providing moral and medical quality control on various levels: (4) setting priorities; (5) setting guidelines for governing use of human research subjects in hospital, nursing homes, home care, and ambulatory settings; (6) setting guidelines in organ-sharing for transplantation in actively promoting organ-sharing on the grass-root level; (7) setting guidelines for confidentiality of results from tests for AIDS, drug dependency, and genetic properties; finally (8) assessing the prime values, virtues and priciples which might this province or community apart from neighboring others.

Research review committees

Clinical research is a noble enterprise in itself, socially not only acceptable but *ethically required* on moral, cultural, religious, and humanitarian grounds. There is no philosophical or religious tradition in the world, that does not support and require mutual aid among fellow-humans, solidarity with the weak and needy, and research for the improvement of support, help and care for those who are sick, suffering, or in pain. In

modern times, strong European humanist and Christian traditions have stewarded and encouraged clinical research for the benefit of the patient and pioneered in the establishment of morally acceptable forms of human experimentation, developing rational and responsible procedures in clinical trials for the protection of research subjects.

Ethically unacceptable forms and goals in research design, such as concentration camp experiments by the Nazis and the Japanese or the Tuskegee syphilis studies in the United States, were the exemption rather than rule and have given rise to heightened ethical awareness and the development and improvement of procedures for good clinical practice in Europe and in most civilized countries. Ethics Committees for clinical research and new therapy have been in force in Prussia since the end of the last century, requiring a responsible balance of harm, risk, and benefit and introducing the principle of informed consent, without which no human experimentation should be allowed and accepted. Since the first introduction of the Helsinki-Tokyo Guidelines for Human Experimentation *review boards* have become a legal requirement for clinical trials all over Europe and in most civilized countries. Principles of 'nonmaleficence'and 'benefit over harm', 'respect for autonomy' and 'informed consent' have become essential features in Good Clinical Practice (GCP).

The mandate of the clinical ethics committees always is to primarily see into the risk-benefit balance, the informed-consent issue. Clinical ethics committees doe not accept responsibility for the actual research which stays with the research teams. Clinical ethical committees in general have are required to include at least one ethicist, one legal expert, one lay person representing the neighborhood, one pharmacologist, and a minimal number of physicians of different subpecialization. But size and membership vary widely. Only a very few clinical ethics committees in Germany have actually philosophers or theologians as members, while their absence in those committees would be unthinkable of in the US. The clinical center at the US National Institute of Health has a rather large number of nine or more members, given the highly specialized research areas; all ethics committee protocols are to be reviewed by the head of the clinical ethics division and signed by the director of the clinical center. Georgetown University Hospital follows another model, having a rather small ethics committee, but decisions are prepared for the ethics committee by expert committees beforehand; the director of the hospital will have to sign the decisions of the ethics committee, and there are cases where he has refused to do so and given the protocol back to the committee and the applicant, mostly because of issues related to informed consent and the language in informed consent forms. As the parameters and duties of clinical

ethics committees are already well established, let me focus on three crucial issues which will overshadow the debate in the future: (1) can ethics be taught and can an expertise in clinical ethics deliberation be developed; (2) are there special requirements for cross-cultural and multinational multicenter studies; (3) has the informed consent principle come to the end of its usefulness and should it be replaced by a more appropriate model such as the 'informed request' model or a 'contract model'?

(1) *Can ethics be taught?* Here is my thesis: *Ethical principles* and bioethical assessment can be taught the same way logic, rational modes of analysis, assessment, and cognitive knowledge can be taught. But *ethical behavior* is an attitude which is as much independent from conceptual analysis as irrational behavior of those who have very well been trained in logic, rational strategy, and assessment of risk. It is well known that knowing the rules and laws does not prevent individuals from violating rules and breaking laws: the better rules are understood, the more sophisticatedly can they be broken, circumvented or bend. Nevertheless, teaching bioethics in the medical and the clinical research setting intends to improve ethical knowledge, assessment skills, and the embodiment of moral attitudes into the day-to-day work of research and clinical care.

If we would live in ideologically closed societies, there would be no need for professional ethical teaching as the role of the professions would be determined by the forces of ideological and political power and ethics would be replaced by exercises in dominance and subordinance. Teaching ethics in a *multicultural environment* therefore is the superior way to assess and to confirm values, virtues, principles, human and civil rights, and to support consensus formation and coordinated action on various levels of private and professional activity. Bioethics, along with other ethics in highly advanced areas of decision making, production, and research, additionally has to face the fact that there are certain ethical challenges, for which traditional moral authorities such as Moses or Jesus, Aristotle or Kant never gave direct guidance, such as for how to deal clinically with human experimentation or genetic predictions, endstage chronic diseases, artificial modes of making babies, or how to treat fellow-humans with irreversible and full brain damage in the presence of highly advanced medical capabilities.

While cognitive knowledge can be taught and learned, attitudinal affirmation or change is more complex and cannot be guaranteed even by the best teaching methods. This is confirmed by a US survey among young physicians who had attended bioethical classes as part of the required clinical curriculum demonstrated that only 3% of them actually changed their system of belief and concept of ethics as a result of those teachings while 94% declared that their attitudes in general have been formed prior to attending professional schools. Their understanding of clinical ethics was strongly influenced by clinical expe-

rience (68%), role model behavior of their clinical teachers (63%), by peer discussion (53%) and by family tradition (58%). As far as specific awareness of issues in clinical ethics were concerned, physicians thought that classes in bioethics improved communication skills with patients (83%), sensitivity in palliative care (52%), partnership with patients in clinical decision making (68%), protecting patient's privacy (56%); but in issues of public controversy bioethics teaching did not change understanding and attitudes: abortion (12%), definition of death (16%), withholding of treatment from severely handicapped newborns (7%) or organ donation (5%). While we have no such empirical data yet from Europe, experiences with mandatory courses in bioethics within medical curricula suggest that results might not be much different. As the majority of medical curricula in the European Community does not have required courses in bioethics yet, it is important to introduce medical humanities into the core curriculum, and also into continuing medical education. Bioethics education for clinical research has to be an essential part of bioethics teaching in general, but additionally there should be specific and highly targeted bioethics training for researchers and research teams, also for members of research ethics committees.

Teaching bioethics in medical education does not intend to compete with teaching philosophy in philosophy departments, but adds skills of moral and cultural analysis and assessment to quality education in medical practice and medical research. Bioethics teaching has *two goals*: (1) It helps physicians and researchers in quality control and quality assurance of care and of research by integrating 'blood status' and *'value status' of the patient* in individualized differential diagnosis and to treat the patient according to her or his individual understanding of quality of life, risk profile, expectations, fears and hopes. Clinical data, ethical principles, and personal data of the individual patient together will form the basis for individualized prognosis, goals of therapy and therapeutic intervention. (2) The *protection of human and civil rights* of probands and patients has to be based on a commonly shared strong bioethical and legal platform, which does not compromise with local customs or cultural attitudes who do not live up to these standards. The European and WHO regulations for GCP define such quality standards, which must not be allowed to be violated even if not protected by national laws or safeguarded by cultural attitudes.

Because of the practical relevance of bioethics teaching, the methods of teaching must primarily be based on case studies, scenario assessment, evaluation of principles, virtues and vices, points-to-consider lists and regulations. It is more important that physicians learn to apply bioethical principles in real-life situations of clinical conflict than mastering the arcane walks in ivory-tower theories of ambiguous authority.

Here is a *seven point list* of concepts which have to be entertained in *bioethics teaching* specific to researchers, regulators, and members of ethics committees: (1) It is not acceptable that investigators or ethics committees force their particular view on values or weltanschauung on others, the least on those vulnerable fellow humans whose life or wellbeing depends on their actions. (2) Basic philosophical or religious have to be left to the individual while basic human and civil right issues, including those regulating clinical research, have to be left to the respective regulatory or legislative authorities. (3) No research can ever be done without appropriate *approval by the research subject*, and the form and content of consent, request, or approval has to be checked carefully, in particular regarding those whose capacity to approve is or might be impaired. (4) Clinical research is a *process* the biomedical, biometrical, and bioethical parameters of which might change during the course of the trial; therefore a one-time punctual review prior to the begin of the trial does not guarantee highest levels of subject protection and quality of the trial. (5) To review the *outcome* of trials not only on biomedical and biometrical grounds but on bioethical grounds as well, is very educational and will improve future trial design and trial procedures. (6) While the four-phase randomized controlled clinical trial (RCT) has become the research model of choice and is supported by a multitude of rules and expectations among researchers, ethicists, regulators, and politicians, *other avenues of research* such investigational new drug trials (IND), participatory models of risk-and-benefit-sharing with patients and probands, and biometrical or biomedical alternatives to human experimentation, including computer simulation, use of historical data, cell-, tissue-, and animal-research, has to become a routine part of the evaluation and education process. (7) Of particular educational and strategic importance is the evaluation of morally *controversial features* such as randomization, double-blind-studies, placebo control versus available alternative drug control, termination of the trial, breaking the code etc.; these challenges occur again in clinical research and therefore should belong to the core topics in bioethics education.

(2) *Ethical challenges in multicenter clinical trials*: As most clinical trials are conducted in multi-center studies, often including centers in different countries regulated by different legal and regulatory parameters and cultural and professional attitudes, the harmonization and quality assurance of bioethical standards is of prime importance and rightly has become the focus of the European Commission. It is self-evident, that good ethical practice in multicenter clinical trials can only be assured by coordinated and integrated bioethics education across the centers and nations involved and by harmonization in the ethical design and quality control of the trial.

Of particular importance is the fair and equal treatment of subjects in multicenter trials across the borders of states and cultures. In biometrical issues we

already enjoy a high degree of coherent and fully integrated statistical quality. We should strive for similar degrees of bioethical quality control and clinical research design. The following *six features* should be considered to implement, to improve, and to harmonize the biometrical as well as bioethical quality and equality of trials: (1) A *bioethics coordinator* or coordinating team, comparable to the coordinator recommended by GCP rules would be charged with coordinating bioethical review and assessment prior, during and after the trial; the coordinator also would be available for acute or routine consultation on bioethical issues at each of the centers for investigators and local review committees. (2) Prior to initiating the trial the development of a specific bioethical *'points to consider' list* and specific case studies would sensitize those involved, speed up the process, and help in creating and improving a common bioethical language and modes of analysis, assessment, and judgment. A bioethics training and harmonization workshop including the heads of local research teams and review boards, the sponsor, insurers and regulators discussing historic cases of comparable moral and medical risk and prospective cases which might occur in the intended trial would improve the strength and design of any large-scale trial. Such a workshop would be imperative if complex cross-national legal and cross-cultural ethical issues are involved. (3) A *concerted action* of centers involved, and including sponsors and whenever possible regulators and insurers, should prior to the beginning of the trials decide on crucial bioethical issues such as (a) placebo control, (b) bioethical and biometrical selection of subjects, (c) language and content of informed consent forms, (d) modification of routine procedures in RCT's and GCP, and (e) define moral and clinical uncertainties regarding risk or harm. (4) While the regulations for GCP require a bioethics review for discontinued trials, it would be extremely educative and would contribute to quality assurance of trials if at the end of all trials *final bioethics review and result report*, together with the biomedical and biometrical results and reports, would routinely be put together. (5) It would also improve design quality and bioethics standards if *informed consent forms* would be developed and tested prior to the beginning of the trial. (6) The *input from research subjects* during and after the trial will be one of the best tools in continuing research ethics training and in improving the bioethical setup of the trial during its course. Also it would be very important to learn from patient's input for future trials of similar bioethical risk; the bioethics literature on clinical research ethics focusses increasingly on issues of patient's input ad response.

The Bochum Center for Medical Ethics has developed a generic points-to-consider list of ten questions, which then will have to lead into the development of more specific lists regarding specific ethical and medical risk of the trial. Here are the ten specific questions: (1) Is the trial design optimal from a

medical-ethical perspective? (2) Is this particular trial necessary? (3) Did the patient give his or her informed consent? (4) Was the information completely or incomplete given or understood? (5) Could there be reasons that consent was not fully voluntary? (6) What principles of justice/fairness were used in selecting patients? (7) Does the patient know about his/her right to terminate participation at any time? Is such termination technically possible? (8) Will there be an ongoing communication with the patient during the trial? Who s personally responsible for continued communication with the patient? (9) Define conflicts between the interest of research, the presumed interest of the patient and interest of the patient as expressed by himself/herself. (9) How do you handle these conflicts of interest? Discuss these conflicts with your patient.

An even more specific list for phase I cytostatica trials has the following four questions: (1) Is your definition of efficiency as expressed in terms of remission or no change in conflict with the patient's definition of quality of life? (2) Which health index profiles or checklists did you use in communicating with the patient? Do you have your own standardized point-to-consider list, especially designed for this particular trial? (3) Is the patient aware of a possible scanty prognosis for full recovery? What does the patient expect form the trial? What does the researcher expect? (4) Has the patient been offered best available palliative care? Has he/she been made aware that best palliative care will continue even if he/she withdraws from the participating in the trial?

(3) *Informed request or a contract model replacing the informed consent principle?*: The discussion of specific ethical issues in multicenter trials raises the question whether or not the traditional informed consent model still is good enough to set the highest possible ethical quality standard. Elsewhere I have proposed to replace the consent model with a contract model. Let me briefly sketch the concept of the contract model.

It has become a routine in GCP and in clinical trial regulation to require *informed consent* of research subjects prior their inclusion in the trial and to inform about their right to withdraw from the trial anytime. The 'informed consent' principle is an essential feature in all clinical trials and required by governmental regulations from the beginning of this century. But just asking for consent is a soft paternalistic principle and not the appropriate expression of the subject's autonomy. Other risky scenarios in the professional and personal setting are handled by principles more appropriate to shared risk and partnership in communication and cooperation: models of '*participatory contract*' or *informed request*. Times and challenges in clinical trials have changed since A B Hill's successfully demonstrated the four-phase model of randomized controlled trials in his 1948 streptomycin research. Today, after decades of successful clinical trials and progress in bioethical reasoning and experience many research issues such as randomization, placebo control, high

risk evaluation, uncertainty assessment and acceptance, data protection, and patient's or proband's benefit cannot be comfortable and ethically handled within such a model of soft paternalism.

Areas of clinical where the traditional model of soft paternalism becomes particularly troublesome include at least the following three: (1) very high medical or moral risk such as adventures in phase I oncological trials in infertility research; (2) issues of data protection and probable benefit or harm which go well beyond the realms of traditional trials involving only the research subject proper and nobody else, such as in predictive genotyping for early health risk recognition and for drug delivery based on individual properties in drug metabolism; (3) issues surrounding the storage of human cells, tissue or other properties for which new avenues of data protection, research subject's benefit, as well as pedigree harm-and-benefit features have to be identified, assessed, and managed in an ethically responsible fashion. Most of these areas will need new forms of risk sharing and new models of communication-in-trust and cooperation-in-trust between sponsors, regulators, insurers, investigators, patients and their families and friends.

Participatory models such as a more formal contractual relationship between subjects and researchers or principles of a more active 'informed request' by the patient rather than the more passive principle of 'informed consent' should be introduced and tested by sponsors, investigators, insurers, and patients, and evaluated by ethics committees and multicenter trial workshops. Therefore, as research ethics committees will have to guarantee, harmonize, and improve the good ethical practice of well established procedures in GCP, bioethics education and training also has to look into new avenues of meeting the bioethical challenges in more recent areas of clinical investigations which warrant new features of participatory responsibility and risk-and-benefit sharing among, sponsors, researchers, regulators, patients and their families.

Hospital ethics committees

Hospital ethics committees are the least known and least widely used instruments to improve the medical and moral quality of patient care on the grassroot level, in the ward, on the bedside. The US journal HEC (for: Hospital Ethics Committees) provides the best insight into the discussions and developments in this field.

In thehospital, we clearly have to differentiate between two types of committees, (1) the *decision making and policy setting committee*, defining the moral character of a hospital or a ward and (2) the consulting committee in individual patient care.

(1) The decision making committee does not address individual cases, rather sets policy and determines the ethical profile of a hospital or a ward. A catholic Hospital, e.g. most likely will set the ethical rule, that abortion are not performed at all or only in the most rare situations of immediate threat of death to the pregnant woman; at the same time a municipal hospital funded by taxpayer's money and being responsible to and serving a wider constituency probably should have at its moral priority to respect the pregnant woman's reproductive choices. It must be normal, that in pluralistic societies rich in different worldviews, beliefs and attitudes different providers of health care offer different sets of values and virtues. The corporate identity and the corporate profile and corporate ethics will be different from institution to institution, thereby serving as a corporate profile to the potential client and patient and as a guidance in educating and training staff, nurses and physicians.

(2) Totally different from the decision making model is the bedside ethics committee evaluating ethical conflicts and ethical requirements in actual individual cases. There seems to be a common understanding that bedside ethics committees should not take away responsibility from attending physicians and their team as this would be counterproductive for good patient care and against the tradition of physician's ethics to accept final responsibility for the individual patient. But bedside ethics committees may serve as a sounding board and discourse medium to analyze issues and conflicts and to evaluate options for individual patient care, thus helping the physician to form and to defend her or his own course of action. Many model of hospital ethics committees have been experimented with and it would lead too far to discuss them all. Also, some hospitals have one or two individual clinical ethics specialists, often a retired senior physician or a priest, performing similar duties as a bedside ethics committee would do.

Instead of a conclusion

In a 1975 review of US Presidential Advisory Commissions from Truman to Nixon Wolanin writes: 'Commissions are uniquely capable of analyzing problems because they are temporary systems; they can recruit well-qualified members and staff; they have unusually good access to expertise and data; and they serve as an integrative framework for an interdisciplinary and multi-interest consideration of problems. Commissions are also particularly capable of persuading others to accept as authoritative the findings and recommendations because they can command a wide audience for their findings....; they have a decision-making process that conforms to the public's ideal of how decisions should be made; and they enjoy the benefits of being both inside and outside

the government.'[p.41] These are quiet positive remarks on public advisory committees; but there are less favorable experiences as well with ethics committees.

From a European perspective, I should balance this positive account with recalling Jean Jaques Rousseau's proposal to differentiate between the *volontee generale* [expressing and formulating human rights and human obligations] and a *volontee de tous* [a majority vote which by its sheer majority or unanimity may call for the most inhuman actions out of mass-hysteria or fundamental ideologies shared by all as the dark days of the inquisition or the holocaust demonstrate quite clearly], reminding us that even unanimous votes by this or that ethics committee does not guarantee good ethical quality nor protection of citizens or patients from exploitation or discrimination.

Common sense teaches that a too easy consensus within a group or committee might not be in the interest of those depending on these anonymous committees. Therefore, a prime ethical and analytical rule for ethics committees in the presence of societal or religious dissent should be to strive for the protection of the individual patient's or citizen's own personal decision in health care matters based on very personal beliefs, goals and values As a golden rule for all sorts of ethics committees one could formulate: as long as and whenever philosophers, theologians, physicians, scientist, lawyers, and politicians of different background disagree, then they have an obligation to form a consensus on the protection of the individual conscience, values and wishes as the true and essential expression of human dignity.

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